Proposed Decision Memo for External Counterpulsation (ECP) Therapy (CAG-00002R2)

Decision Summary

The Centers for Medicare and Medicaid Services (CMS) is seeking public comment on the proposed determination that the evidence is not adequate to conclude that external counterpulsation therapy is reasonable and necessary for:

- Canadian Cardiovascular Society Classification (CCSC) II angina
- Heart Failure
  - New York Heart Association Class II/III stable heart failure symptoms with an ejection fraction of ≤ 35%
  - New York Heart Association Class II/III stable heart failure symptoms with an ejection fraction of ≤ 40%
  - New York Heart Association Class IV heart failure
  - Acute heart failure
- Cardiogenic shock
- Acute myocardial infarction

Current coverage as described in Section 20.20 of the Medicare National Coverage Determination (NCD) manual will remain in effect.

We are requesting public comments on this proposed determination pursuant to Section 731 of the Medicare Modernization Act. After considering the public comments and any additional evidence we will make a final determination and issue a final decision memorandum.

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Proposed Decision Memo

TO: Administrative File: CAG-00002R2
External Counterpulsation Therapy

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SUBJECT: Proposed Coverage Decision Memorandum for External Counterpulsation Therapy
DATE: December 20, 2005

I. Proposed Decision

The Centers for Medicare and Medicaid Services (CMS) is seeking public comment on the proposed determination that the evidence is not adequate to conclude that external counterpulsation therapy is reasonable and necessary for:

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II. Background

External counterpulsation is a non-invasive procedure that can be used to treat various conditions on an outpatient basis. For this proposed decision the requestor is seeking extended coverage for certain cardiac conditions (as the device is also used for other medical conditions that are not cardiac conditions), where the intended clinical result of external counterpulsation (ECP) is to increase the heart's oxygen supply while decreasing its oxygen demand. ECP systems consist of inflatable pneumatic-compressive cuffs, valves, and compressors synchronized with an electrocardiograph (ECG). These devices inflate and deflate a series of pneumatic-compressive cuffs enclosing the lower extremities. Treatment occurs on a padded table in which three sets of electronically controlled inflation and deflation valves are located. These valves connect to adjustable cuffs that wrap firmly around the patient's calves, lower thighs, and upper thighs including the buttocks. External pressure is applied to the patient through inflation of the cuffs. In early diastole, pressure is applied sequentially from the lower legs to the lower and upper thighs to displace a volume of blood back to the heart. Then, when the left ventricle contracts and the cuffs deflate, aortic pressure is reduced as the volume of blood upstream of the cuffs fills the lower extremities. Pressure settings can be varied to effect certain blood pressure changes during treatment, with the blood pressure monitored by finger plethysmography. Treatments are usually given in one-hour sessions once or twice a day and a full course of treatment is typically defined as 35 hours.

Though studies investigating the mechanism of action date to the 1960s, the exact physiologic mechanism remains unclear.

III. History of Medicare Coverage

Prior to July 1, 1999, a national non-coverage policy for all uses of ECP was delineated in Section 35-74 of the Medicare Coverage Issues Manual (CIM).

In April of 1999, after review of a published randomized study, the MUST-EECP trial, Section 35-74 was amended to remove the national non-coverage policy previously in place and allow coverage for this procedure under certain circumstances. Coverage for ECP was only provided for patients who have been diagnosed with disabling angina (Class III or Class IV, Canadian Cardiovascular Society Classification or equivalent classification) and who, in the opinion of a cardiologist or cardiothoracic surgeon, are not readily amenable to surgical intervention. This change became effective July 1, 1999.

Also, effective July 1, 1999, the name for this procedure was changed to "Enhanced External Counterpulsation (EECP)." The Centers for Medicare and Medicaid Services (CMS), formerly the Health Care Financing Administration (HCFA), based this change on the information presented by Vasomedical, Inc., which referred to its device as the "Enhanced External Counterpulsation (EECP®) System" and the name of the therapy as "Enhanced External Counterpulsation." Additionally, the majority of the medical literature regarding this procedure refers to EECP, and the MUST-EECP study was conducted using devices supplied by Vasomedical, Inc.

Soon after this decision, another manufacturer, Cardiomedics Inc., presented information about the EECP terminology used in the CIM. Cardiomedics Inc. objected to the use of this trademarked term, suggesting that CMS alter the language of the instruction so that coverage of this treatment would not exclude manufacturers other than Vasomedical. CMS accepted Cardiomedic's formal request to reconsider this decision on July 9, 1999.

On October 6, 1999, CMS accepted a request for reconsideration of the entire EECP policy submitted on behalf of the Medicare Contractor Medical Director New Technology Workgroup, which believed that there was not sufficient evidence to permit coverage. The two requests were combined. After review, the positive coverage decision remained in effect and the CIM was amended to remove any reference to the trademarked term EECP and to remove language which had limited coverage of this therapy to specific ECP systems.

On April 11, 2001, CMS accepted a request from the Circulator Boot Corporation to reconsider the ECP policy. In its request, the Circulator Boot Corporation pointed out that the original evidence considered for this (ECP) policy did not support CMS' statement that "other uses of this device and similar devices remain non-covered." This request was based on the contention that CMS had misinterpreted the ECP evidence to include non-coverage of other end diastolic pneumatic compression devices cleared by the FDA for non-cardiac conditions. Furthermore, the Circulator Boot Corporation pointed out that CIM 35-74 explicitly defines ECP as a non-invasive outpatient treatment for coronary artery disease refractory to medical and or surgical therapy, with no specific mention of coverage or non-coverage for other non-cardiac indications. At the core of its request, the Circulator Boot Corporation contended that the Circulator Boot was designed for the treatment of vascular diseases of the lower extremity and therefore differs significantly from ECP devices that are designed for the treatment of cardiac conditions.

According to the 510(k) summary information included in the FDA's clearance letter dated August 14, 1997, the Circulator Boot was found to be equivalent to the original Circulator Boot, the Jobst Extremity Pump, and the Cardiassist ECP device. Note that devices with similar FDA classifications do not necessarily imply that the clinical indications of the devices are the same.

After a review of this reconsideration request, CMS concluded that the policy set forth in CIM section 35-74 should be limited to ECP devices intended for the treatment of cardiac conditions. Other non-cardiac conditions in which end diastolic pneumatic compression devices may be considered for coverage are not considered under this policy. Therefore, Medicare contractors would continue to have discretionary authority in making reasonable and necessary coverage determinations related to other end diastolic pneumatic compression devices not related to this policy or included in any other section of the CIM. CIM 35-74 was amended to indicate that this policy **only** pertains to ECP devices intended for the treatment of certain cardiac conditions.

Current Request

On June 20, 2005, CMS accepted a request from Vasomedical Inc. to reconsider the ECP policy. In this reconsideration, Vasomedical Inc. is requesting that CMS expand coverage of ECP to include treatment of patients with Canadian Cardiovascular Society Classification (CCSC) II angina and for use in patients with New York Heart Association (NYHA) Class II/III stable heart failure symptoms with an ejection fraction of $\leq$ 35%.

On June 23, 2005, CMS also received a request from Cardiomedics to reconsider the ECP policy. Cardiomedics requests expansion of coverage to include 1) treatment of congestive heart failure, to include NYHA Class II, III with a left ventricular ejection fraction (LVEF) $\leq$ 40%, and acute heart failure; 2) treatment of stable angina to include CCSC II angina; 3) treatment of acute myocardial infarction; 4) treatment of cardiogenic shock. On September 15, 2005, Cardiomedics amended their request to include NYHA Class IV heart failure.

CMS is evaluating both requests in this analysis.

On December 14, 2005 Cardiomedics, during a meeting with CMS, requested to amend their request and withdraw the request for coverage for acute congestive heart failure and to include coverage for acute myocardial infarction where percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass graft (CABG) is not available. Due to the lateness of this request and the inclusion of both congestive heart failure and acute myocardial infarction in our analysis, CMS does not feel it is necessary to amend the analysis at this time.

Benefit Categories

Medicare is a defined benefit program. An item or service must fall within a benefit category as a prerequisite to Medicare coverage. §1812 (Scope of Part A); §1832 (Scope of Part B); §1861(s) (Definitions of Medical and Other Health Services). External counterpulsation therapy is eligible for coverage under §1861(s)(1), Physicians Services.

IV. Timeline of Recent Activities

May 31, 2005	Vasomedical Inc. submitted a cover letter and supporting documentation requesting that CMS expand coverage indications for external counterpulsation therapy.
June 20, 2005	CMS opened the National Coverage Determination (NCD) process based on Vasomedical's request. Tracking sheet was posted to web site. Public comment period for 30 days begins.
June 29, 2005	Tracking sheet amended to include Cariomedics' request Public comment period extended to July 29.
July 29, 2005	Public comment period closes.
August 29, 2005	Meeting with Vasomedical.

September 15, 2005	Cardiomedics submitted letter to amend their request.
December 14, 2005	Meeting with Cardiomedics.

V. FDA Status

The FDA approved the CardiAssist™ ECP system for the treatment of angina, acute myocardial infarction and cardiogenic shock under a 510(k) submission in 1980 (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm?ID=27072). Since then, additional ECP devices have been cleared by the FDA for use in treating stable or unstable angina pectoris, acute myocardial infarction, cardiogenic shock, and congestive heart failure.

VI. General Methodological Principles

When making national coverage decisions, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service is reasonable and necessary. The overall objective for the critical appraisal of the evidence is to determine to what degree we are confident that: 1) specific clinical questions relevant to the coverage request can be answered conclusively; and 2) the extent to which we are confident that the intervention will improve net health outcomes for patients.

We divide the assessment of clinical evidence into three stages: 1) the quality of the individual studies; 2) the relevance of findings from individual studies to the Medicare population; and 3) overarching conclusions that can be drawn from the body of the evidence on the direction and magnitude of the intervention's risks and benefits. The three stages of assessment are detailed in Appendix 1.

The methodological principles presented here represent a broad discussion of the issues we consider when reviewing clinical evidence. However, it should be noted that each coverage determination has unique methodological aspects.

VII. Evidence

A. Introduction

Ideally, the goal of external counterpulsation treatment should be to reduce symptoms, decrease morbidity, and potentially improve mortality by reducing ischemia through favorably impacting myocardial oxygen supply and demand. Traditional outcomes (whether or not a patient benefits from the medical care provided) that reliably affect morbidity and mortality are outcomes of interest to CMS. Other measures of interest can also include quality of life and related to this, patient symptoms. Rigorous research design leads to the most convincing and dependable outcome results. A randomized trial best demonstrates the effectiveness of an intervention, serving to protect against selection bias (choosing subjects with certain attributes that may unduly influence the outcome) in the assignment process, and assuring that the degree of baseline comparability for an unobserved variable is the same as for the observed variable. Additionally, to determine if a treatment leads to the subsequent outcome, comparison groups (controls) are necessary. Case study or case series lacks a comparison with an untreated group or with a group receiving some other treatment. Evidence about whether the treatment directly causes the subsequent outcome (or whether there is something else that actually causes the outcome) cannot be discerned.

Clinical outcomes including functional classification of angina pectoris, Canadian Cardiovascular Society Classification (CCSC), daily anginal counts, and nitroglycerin use are most often reported in ECP studies. While improvement in angina is important, angina (pain) is subjective and is also subject to the phenomenon of regression to the mean (level of perceived pain has a tendency to naturally fluctuate about a mean value, which is the average of the level of pain). It is known that the perception of pain varies from individual to individual, without knowing why this fact is so. As an extreme example, some patients have silent heart disease, and we do not know why they lack pain but have obvious disease. Conversely, other patients have chest pain that is identical to angina, but no reason can be found for the pain when diagnostic studies are performed. Some investigators believe that various factors influence the perception of pain, such as age, sex, and psychological and psychosocial factors, for example. The threshold for pain can also vary within the same person based on environmental and psychosocial factors. Therefore, measuring symptom reduction may not be the same thing as measuring ischemia reduction.

While CCSC is a standard for grading angina in patients with chronic stable angina, the relationship between CCSC and the severity of coronary artery disease (objectively measured by coronary angiography) is not clear. A recent article suggests that the Canadian Cardiovascular Society Classification of exercise angina is not a reliable surrogate for the severity of coronary artery disease, as there has been shown generally little correlation between exercise angina class and angiographic findings (the only positive findings were that class I patients had less left main disease than class IV, $p = 0.02$, and class IV patients had fewer normal coronary angiograms than class I, $p = 0.001$).[1] It is for these reasons that CCSC, daily anginal counts, and nitroglycerin use alone are not sufficient outcomes for determination of evidence of benefit.

In some studies of ECP, cardiovascular stress testing has also been done pre and post treatment. This type of diagnostic testing attempts to elicit cardiovascular abnormalities that are not present at rest to help determine the adequacy of cardiac function for risk or prognostic stratification. There are several stress tests with a variety of variables that can be measured. As with any diagnostic testing, it is important to be able to understand what the results of the test mean. Cardiovascular stress testing can be physiological stress by exercise testing that use treadmill or bicycle exercise and electrocardiographic and blood pressure monitoring, or pharmacological stress which commonly includes the use of imaging modalities (such as radionuclide imaging and echocardiography). The American Heart Association has produced a guideline for clinical exercise testing laboratories.[2] This guideline recommends that exercise testing protocols be chosen based on the limitations of the individual, with the desired testing end point reached within 8 to 12 minutes of testing. It further states:

“The demographic data, date of test, and protocol used should be clearly identifiable. The report should include the peak work rate achieved by the patient in METs or VO_2, peak heart rate and blood pressure, and any abnormal signs or symptoms that occurred during or after the test. The ECG data should consist of rest, abnormal exercise changes, and return to baseline. Occurrence of arrhythmias must be noted as well. If ischemia was demonstrated by ECG changes, the time and double product at which the changes initially occurred should be specified. If gas exchange measurements were made, peak oxygen uptake, ventilatory threshold (if achieved), and level of effort should be reported.”

For interpretation of the exercise test, the above noted information is recommended. It is important to note abnormalities in exercise capacity, systolic blood pressure response to exercise, and heart rate response to exercise. An important prognostic marker identified in exercise testing is maximum exercise capacity, which is influenced by left ventricular dysfunction. The relationship of exercise capacity and left ventricular function is not without other contributing factors. Exercise capacity is affected by age, general physical conditioning, comorbidities, and psychological state.[3] Several measures can be used as markers of exercise capacity, including maximum exercise duration, maximum MET level achieved, maximum work-load achieved, maximum heart rate, chronotropic incompetence, and double product (rate times pressure).[3,4] When exercise testing is being interpreted, it is important that exercise capacity be taken into account. The translation of exercise duration or workload into METs (oxygen uptake expressed in multiples of basal oxygen uptake, 3.5 O_2 mL/kg per minute) provides a common measure of performance regardless of the type of exercise test or protocol used. Importantly, the guideline mentions that risk stratification with the exercise test does not occur in isolation. Exercise testing for risk stratification must be viewed in the context of the patient’s other known risk factors.[3]

One of the premises of ECP treatment is that effective diastolic augmentation (DA) (the increase of arterial blood pressure and retrograde aortic blood flow during diastole) is an important treatment parameter, as this has been hypothesized to be the main mechanism of effect by some.[5] To quantify DA, blood pressure changes are monitored by finger plethysmography. Two ratios are computed, using the systolic and diastolic peak pressures or the area under the systolic and diastolic curve. Ratios greater than one indicate that diastolic pressures are greater than systolic pressures. It has been suggested that for optimal hemodynamic effects the DA should be in the range of 1.5 to 2.0.[5,6] While the DA ratio is commonly measured, it has not been clearly correlated with decreased morbidity or mortality, or with symptoms or quality of life improvement. Given the current knowledge, diastolic augmentation is not a sufficient outcome to determine the adequacy of the evidence.

Factors that reliably affect morbidity and mortality are heavily weighted outcome measures for CMS’s analysis of the evidence for a national coverage determination. Morbidity measures of interest include adverse events associated with treatment, subsequent clinical events including illness exacerbation, and hospitalizations and procedures for the condition under study and related conditions. When reporting either morbidity or mortality, it is important to consider potential confounding factors, such as severity of illness and co-morbidities.

Other issues of importance are long-term outcomes and generalizability to the Medicare population.

The outcome relationship to treatment effect is evaluated with the thoughtful application of statistical tools. The goal of most statistical analysis is to form valid conclusions about a population that is based upon information obtained from a sample of that population. A variety of methods exist for analysis. The choice of an appropriate method depends on the purpose of the research as well as the types of variables under investigation.[7] Data analysis should have a rational for choosing a particular method of analysis.[7] Additionally, as Kleinbaum, et al., states, “The finding of a “statistically significant” association in a particular study (no matter how well done) does not establish a causal relationship.”[7] Further, statistical significance should be viewed in the context of clinical significance, for even though a variable may be found to be statistically significant, it may lack clinical significance.

B. Discussion of evidence

1. Questions:

The development of an assessment in support of Medicare coverage decisions is based on the same general question for almost all requests: "Is the evidence sufficient to conclude that the application of the technology under study will improve net health outcomes for Medicare patients?" For this NCD, the question of interest is:

Is the evidence sufficient to conclude that the Medicare population will have net health benefits for the following conditions as a result of treatment with external counterpulsation therapy?

- Canadian Cardiovascular Society Classification (CCSC) II angina
- Heart Failure - New York Heart Association Class II/III stable heart failure symptoms with an ejection fraction of $\leq$ 35%
  - New York Heart Association Class II/III stable heart failure symptoms with an ejection fraction of $\leq$ 40%
  - New York Heart Association Class IV heart failure
  - Acute heart failure
- Cardiogenic shock
- Acute myocardial infarction

2. External Technology Assessment

No external technology assessment was commissioned.

3. Internal Technology Assessment

Vasomedical and Cardiomedics initially provided 15 articles to review for this coverage determination (1 randomized controlled trial, 10 case series reports, 1 trial design, 1 editorial and 1 review). On September 29, Vasomedical provided one previously published article (review) and several other draft articles (one of which was published in the interim) and an abstract. On September 30, Cardiomedics provided a draft article CMS conducted an independent literature review. Pub Med was searched using combinations of the following terms: enhanced external counterpulsation; external counterpulsation. Google was used for a search using these terms: external counterpulsation; external counterpulsation assessment. No other randomized controlled trials were found. Forty-four other articles were found that included case series (including registry data) and reviews.

Much of the case series data comes from the International EECP Patient Registry (IEPR), which is used to track acute and long-term outcomes for consecutive patients treated for chronic angina. The IEPR began in January 1998 and enrolls patients from > 100 centers in the United States and other countries. The criteria for entry are that the patient give informed consent and have ≥ 1 hour of EECP treatment for chronic angina. There are over 7,500 patients in the registry.

Evidence Summary

Indication 1: Stable Angina

Most of the published studies concern patients with stable angina. As no separate studies on Class II angina have been published, stable angina will be discussed.

Randomized Controlled Trial Study Design

One published randomized controlled trial for angina, the MUST-EECP trial,[8] has been reported to date.

In this trial, participants were randomized and blinded. Medical staff applying the treatment were not blinded. The study had multiple exclusionary criteria:

- MI or CABG in the preceding three months,
- cardiac catheterization in the preceding two weeks,
- unstable angina,
- overt congestive heart failure or a left ventricular ejection fraction ≤ 30%,
- significant valvular heart disease, blood pressure > 180/100 mm Hg,

- permanent pacemaker or implantable defibrillator,
- non-bypassed left main stenosis greater than 50%,
- severe symptomatic peripheral vascular disease,
- history of varicosities,
- deep vein thrombosis,
- phlebitis or stasis ulcer,
- bleeding diathesis,
- warfarin use with International Normalized Ratio > 2.0,
- atrial fibrillation or frequent ventricular premature beats that would interfere with EECP triggering or baseline electrocardiographic abnormalities that would interfere with interpretation of exercise electrocardiogram,
- subjects unable to undergo treadmill testing, and
- subjects enrolled in a cardiac rehabilitation program or in another research program.

Patients had symptoms consistent with Canadian Cardiovascular Society Classification angina levels I, II, and III. Control was a sham pressure of 70 mm Hg versus the treatment pressure of 300 mm Hg. There were 72 patients in the active ECP group, with 59 completing the trial. Complete data were not available for the 59 who completed the trial as patient numbers differed for the various outcomes. In the sham ECP group, 67 were randomized and 65 completed the trial. Again, patient numbers varied for the outcomes, with only 56 being included in the exercise time to ST-segment depression from each group. It is not clear if the patients who were excluded from analysis are equivalent to those who were included. The end points were:

1. Exercise duration:
   Exercise duration was defined as elapsed time from the initiation of exercise to the beginning of the recovery period as read from the tracing of the exercise treadmill test (ETT). The baseline ETT used either a standard or a modified Bruce protocol and was performed within four weeks of treatment initiation. For the follow-up ETT, “a post-treatment ETT was performed” without details. Baseline and post-treatment ETT were performed by blinded personnel.

2. Exercise treadmill time to $\geq$ 1 mm ST-segment depression:
   Time to ST-segment depression was defined as the elapsed time from initiation of exercise to the occurrence of horizontal or down-sloping ST-segment depression $\geq$ 1 mm, 80 ms after the J point, persisting for at least three consecutive beats. As above, baseline ETT used a standard or a modified Bruce protocol. For the follow-up ETT, “a posttreatment ETT was performed” without details.

3. Average daily anginal attack count:
   The average frequency of angina episodes per day (angina counts) was computed by dividing the total number of angina episodes reported at three successive treatment sessions by the number of days in which the sessions took place. The first three sessions were considered the baseline period. The difference in angina counts between baseline and at end-treatment were calculated as percentage change for each patient in the active- and inactive- ECP groups and were then classified categorically.

4. Nitroglycerin usage:
   The analysis of average usage of on-demand nitroglycerin tablets per day was accomplished similarly to the analysis of angina counts, without using categorization in this analysis (reason not given).

Table 1. Study Endpoint Results

	Treatment Group		Control Group		p
	Baseline	Post-Rx	Baseline	Post-Rx	
Exercise Duration (sec)	426 ± 20	470 ± 20	432 ± 22	464 ± 22	> 0.3
Time to ≥ 1-mm ST-segment depression (sec)	337 ± 18	379 ± 18	326 ± 21	330 ± 20	= 0.01
Mean change in angina counts	0.76 ± 0.15	0.55 ± 0.27	0.76 ± 0.13	0.77 ± 0.2	< 0.09
Mean change in nitroglycerin usage	0.47 ± 0.13	0.19 ± 0.07	0.51 ± 0.15	0.45 ± 0.19	> 0.1

Exercise duration was 426 ± 20 seconds at baseline and 470 ± 20 seconds post-treatment in the treatment group and 432 ± 22 seconds at baseline and 464 ± 22 seconds post-treatment in the control group, with no statistical significance between groups when the group mean increase is compared (see Table 1). Time to ≥ 1-mm ST-segment depression was 337 ± 18 seconds at baseline and 379 ± 18 seconds post-treatment in the treatment group and 326 ± 21 seconds at baseline and 330 ± 20 seconds post-treatment in the control group, with statistical significance between groups when the group mean increase is compared (difference of 49 seconds between groups). The difference between groups in the change in angina counts from baseline to post-treatment was not statistically different. The authors then chose to examine angina counts categorically, grouped by percentage improvement or worsening. This categorical outcome did show a p value of < 0.05. The difference between groups in change in nitroglycerin usage from baseline to post-treatment was not statistically significant. In the treatment group, 54.9% (39 of 71) had an adverse experience, while 25.8% (17 of 66) in the sham treatment group had an adverse experience. Adverse experiences that were reported as non-device related (15 in the sham group, 33 in the treatment group) included other chest pain (3 in sham group, 7 in the treatment group), A/V arrhythmia (3 in the sham group, 9 in the treatment group), and respiratory (2 in the sham group, 4 in the treatment group). Adverse experiences that were device related (10 in the sham group and 37 in the treatment group) included skin abrasion, bruise, and blister (2 in the sham group and 13 in the treatment group) and pain (legs, back) (7 in the sham group, 20 in the treatment group).

Seventy-one of the original MUST-EECP patients (54% follow-up) provided health-related quality of life (QOL) information through a mailed questionnaire at 12 months post-treatment.[9] Information was collected at baseline before treatment, at the end of treatment, and one year following the end of treatment. Interestingly, both treatment and control groups had improvement in baseline to end of treatment, with the differences between the two groups reported as being statistically significant only for one of the 4 selected parameters. Baseline to 1-year follow-up comparison shows statistical significance between treatment and control groups in bodily pain, social functioning and cardiac specific health and functioning. Baseline data for QOL scores of treatment and control were not provided. Change from baseline to end of treatment and change in baseline to 1 year following end of treatment for the group as a whole was presented. The values at end of treatment or 1 year follow-up were absent. The sample size in this study was set by follow up from the previous trial, not by the power to detect difference. Data were not correlated with the previous data from exercise testing or anginal symptoms. The decrease in anginal episodes reported at the end of active treatment was not reported for the one year outcome.

Case Series Study Design

Extended Prognosis

A 2000 study evaluated the extended prognosis (4 to 7 years) after treatment with external counterpulsation in 33 non-randomized patients with angina.[10] Patients were all treated with ECP (35-36 hours, pressures not listed) and had a radionuclide stress perfusion imaging, both pre and post-treatment. On the basis of imaging improvement after treatment, patients were divided into groups of either responders or nonresponders. The responder group had 26 patients, with 7 in the nonresponder group. The differences in the nonresponders versus the responders were not clear other than 43% of the nonresponders had diabetes, versus 12% of responders, and 100% had multivessel disease, versus 68% of responders. Follow-up treatment decisions were not uniform, but were made by the patient and physician and between group differences are not reported. Post-treatment, anginal symptoms decreased in all patients. Radionuclide stress tests (performed to the same cardiac work load and double product pre and post ECP treatment) demonstrated improvement in perfusion defects in 26 of 33 patients (responders). Stress perfusion defects in the remaining seven patients were unchanged post treatment (nonresponders). A decrease in antianginal medication use was seen in 31% of the responders and in 43% of the nonresponders (p = NS). Over the subsequent course of follow-up, mortality or a major adverse cardiac event (MACE) occurred in 6 of 7 patients in the nonresponder group, and in 6 of 26 patients in the responder group (p < 0.01). Nonresponders had higher major adverse cardiac events. Although patients were followed between 4 to 7 years, it was not clear what determined the follow-up time other than occurrence of outcomes of interest, death or MACE.

A 2005 case series study examined the predictors of benefit in angina one year after therapy and compared initial responders to nonresponders, as defined by those patients with a reduction of at least one CCS angina class after ECP (responders) and those not showing reduction in angina (nonresponders).[11] From a series of 2,007 patients completing at least 30 hours of ECP, 82.7% were classified as responders. At one year 35.4% of initial nonresponders and 70.6% of responders remained improved by at least one angina class and free of major adverse cardiovascular events (it was not clear if those who were excluded, including those who did not finish treatment, differed from those included in the study). The study listed multivariate predictors of 1-year benefit as initial response to treatment and baseline angina class compared with class IV (odds ratios; class I 2.1, 95% CI 0.93-4.81; class II 0.62, 95% CI 0.43-0.87; class III 0.80, 95% CI 0.62-1.01). In essence, Class I responded better than IV (no statistical significance), class II responded worse that class IV, as did class III (no statistical significance); thus demonstrating no simple trend from a large series of patients. When comparing adverse outcomes, the nonresponders had higher rates of death, MI, CABG, PCI, CABG or PCI, and MACE. Nevertheless the authors concluded, “despite the lack of initial response, that the nonresponders still demonstrate benefit over their baseline status at 1-year follow-up.” They also noted: **“**It is probable that there is a significantly positive benefit to the 30 or more hours of contact patients experienced. It has been well demonstrated that recurrent patient visits may improve health and quality of life measures as an independent variable.”

Medicare Population

One article compared IEPR data for those above 80 years of age to those below that age.[12] This study analyzed 3,037 patients including 249 octagenerians from 80 centers in the US and abroad. Entry criteria are listed as informed consent and at least 1 hour of ECP treatment for angina, but an analysis of those excluded is not given. Fewer patients in the octagenerian group completed therapy as compared to younger patients (76% vs. 84%; $p < 0.01$) with the authors noting “failure to complete a course of treatment in the elderly population was frequently due to an intervening non-cardiac medical event or patient choice.” These patients who failed to complete treatment were excluded from the analysis. It is not clear how these patients differed from those who were analyzed. Of those who completed treatment, the authors report a 76% reduction in angina class “by greater than or equal to one class”(follow-up time for this measure is listed as “post treatment” but it is not clear when following treatment this measure was taken).[12] Weekly angina episodes and nitroglycerin use were decreased by six episodes in the elderly but the statistical significance of this difference is not given and again it is not clear when after treatment this measure was taken. Only 57% of the elderly were on beta blockers, 69% were on aspirin, and 46% were on lipid-lowering therapy, although the authors state that patients referred for ECP were considered optimally medically managed. They also state that no attempt was made to maintain current medication regimens during the study, so it was possible that medications and other therapies were changed during the course of ECP therapy. It was reported that assessed quality of life, health and satisfaction were improved post-treatment ($p < 0.001$ for each), but it is unknown if validated measures were used as the data were reported only by a bar graph with the percent of patients who reported good, very good, or excellent on each measure before and after ECP. Six-month follow up of 183 patients was done during a telephone interview, with 81% reporting maintenance of angina improvement.

Morbidity

A retrospective study of 58 patients with CCSC class II, III or IV who met inclusion/exclusion criteria were treated with standard ECP (35 one-hour sessions with cuff pressures of 250-310 mm Hg).[13] The authors listed five outcomes. For CCSC, the pretreatment functional class was 2.67 ± 0.71 and the post-treatment functional class was 1.71 ± 0.65, with a p value listed as 7.32×10^{-12}. The study did not make clear the difference between a functional class of 2.67 versus 1.71, other than statistical significance. Percent improvement in angina symptoms was given, with no pre and post comparison, as 42% having 50+ % improvement, 11% having 25% - 49% improvement, and 5% having 0% to 24% improvement. The average number of angina episodes over 24 hours pretreatment was 1.59 ± 2.86 and post-treatment was 0.31 ± 0.57. Sublingual nitroglycerin consumption per day pretreatment was 0.62 ± 0.71 and post-treatment 0.14 ± 0.33. Only 24 patients were included in the analysis of hospitalizations for angina per patient over 6 months of follow-up. Hospitalizations pretreatment were 1.17 ± 0.38 and post-treatment 0.04 ± 0.20 (apparently some who were not hospitalized pretreatment were hospitalized post-treatment) with the p value listed as 1.02×10^{-16}. Hospitalizations for other causes such as congestive heart failure were not listed or compared.

Perfusion studies

In a study published in 2003, 25 patients treated with ECP underwent an exercise test with a Bruce protocol comparing SPECT scans pre- and post- ECP treatment.[14] There were no controls. ECP (done in "standardized fashion") post-treatment measures showed an improvement in heart rate-blood pressure product of 18,891 ± 3,939 to 20,464 ± 4,305 ($p < 0.03$), and a reduction in radionuclide perfusion score by ischemic segments (16.36 ± 10.52 to 14.12 ± 10.9, $p < 0.05$). Most patients (21 of 25) had a reduction in at least one angina class. More than half of the patients (16 of 25) had improved nuclear scores on the stress study exercise time (449.3 seconds compared to 357.2 seconds pre-ECP, with one apparently significant outlier). The clinical significance of these changes was not discussed. There were 16 of 25 patients with ST-segment depression on the pre-ECP exercise treadmill test. Post ECP, 3 of those 16 patients had no ST-segment depression on their ETT and 10 of the 16 patients had a statistically significant delay in their time to ST-segment depression (though there appeared to be one extreme outlier). Inclusion criteria included the capability of exercising on a treadmill according to a Bruce protocol, and it was mentioned that it was not possible to eliminate an exercise training effect.

In 2001, investigators in Japan reported on 12 patients with documented ischemia (8 patients had functional angina and 4 patients had silent myocardial ischemia) who while hospitalized underwent 35 sessions of ECP and had exercise thallium-201 scintigraphy, gated blood pool cardiac scintigraphy and cardiac catheterization before and after treatment.[15] Exclusion criteria were the same listed as for MUST-EECP. The investigators described a control period of 38 ± 9 days during which the patients were in the hospital and engaged in sedentary or mild activity. Baseline testing was performed during this time. The next phase of treatment was 35 hours of ECP given once or twice per day, for a total of 36 ± 6 days. In this study, the cuff pressure was set at 300mm Hg, with a mean diastolic to systolic pressure ratio of 1.1 ± 0.4. Exercise thallium was performed at the same cardiac workload before and after treatment. Values were presented as means standard deviation or percentages. Comparisons used paired Student t-test, and multiple comparisons were analyzed by repeated measures analysis of variance. Exercise parameters (exercise duration, exercise tolerance, time to 1-mm ST segment depression, rate pressure product at peak exercise and a 1-mm ST segment depression) were not significantly different at baseline or before treatment but improved after treatment ($p < 0.05$). Myocardial perfusion abnormalities decreased after treatment (50% to 33%, $p < 0.01$). The plasma levels of brain naturetic protein decreased after treatment ($p < 0.05$). Left ventricular systolic and diastolic function was assessed by cardiac cath and noninvasive radionuclide angiography. Ejection fraction systolic indexes were not changed. Left ventricular end diastolic pressure decreased and diastolic indexes improved after treatment. It is of note that no patient during this study experienced angina, which seems to be attributed to the fact that they were in the hospital. No explanation was provided how hospitalization eliminated angina episodes.

In a study published in 2002, the International Study Group enrolled 175 patients (case series) (88% men, mean age 61 ± 9.5 years), apparently over a period of 7 years.[16] Patients had a baseline pre-ECP radionuclide perfusion treadmill stress test (RPST) within a month before ECP and then within 6 months of completing ECP treatment. The maximal external compression used in this study was 225 to 275 mm Hg. Anginal medication adjustment was determined by patients and their physicians, and the changes were documented (it was not stated what they were controlled for in the final analysis). 85% reported improvement in angina of $\geq$ 1 CCS angina class, 15% reported improvement by $\geq$ 2 classes. Post exercise tests were to two different endpoints – one to the same level of exercise pre and post ECP, and the other to maximal cardiac workload post ECP. In centers that exercised to the same level pre and post ECP, 83% had improvement in RPST perfusion defects; 16% had no improvement. No correlation for angina symptoms was given (also, data and statistical significance were not given for the RPST). In this group of patients, the post exercise time was not statistically significant from the pre-exercise time, and the double product (blood pressure X heart rate) decreased ($p < 0.05$). The lower double product was reported as "analogous to the peripheral vascular conditioning effect seen with exercise, in which improved vasomotor tone decreases the blood pressure response to exercise." In patients who underwent post ECP maximal RPST, exercise duration improved (6.61 ± 1.88 minutes pre-ECP versus 7.41 ± 2.03 minutes post-ECP, $p < 0.0001$), with no change in double product. In this group, 54% showed improvement in RPST defect, 42% had unchanged defects, and 3% had a worsening.

A study in 2004 looked at the effect of enhanced external counterpulsation (at least 35 one-hour sessions at 300 mm Hg cuff pressure) in 23 consecutive patients with angina who had a positive dobutamine stress echocardiogram.[17] "Established exclusion criteria" were used. In this study, 10 patients had an improvement of $\geq$ 2 grades in the stress-induced wall motion score, whereas the remaining 13 did not show improvement. Interestingly, those who showed improvement on the dobutamine stress echocardiogram had a greater increase in diastolic augmentation ratio (1.2 ± 0.6 versus 0.5 ± 0.5, p = 0.01), but the CCS angina class results after enhanced external counterpulsation and exercise comparison between the two groups had non-significant p values.

In 2001, a study examined the psychosocial effects of ECP treatment on 27 patients, and included pre and post ECP thallium scans.[18] Of the 27 patients, 17 were categorized as "improved" on myocardial perfusion on stress thallium post ECP in that reversible defects were resolved, and 10 of 27 had unchanged perfusion scans. Both the improved and unchanged groups rated overall well-being as improved, as was chest pain frequency per week, chest pain severity, and nitrate use frequency per week. Results were statistically significant whether or not there was an improvement in the thallium scan. In examining the psychosocial effects of ECP, there was improvement in levels of depression, anxiety and somatization, but no change in levels of anger or hostility for either group of patients. The authors concluded that "on most measures, change was more significant for subjects who showed objective evidence of resolution of ischemia".

Hemodynamic effects

A 2001 study examined 1,004 IEPR patients for diastolic augmentation (DA) as it had been proposed that maximum hemodynamic effects occur when the ratio of diastolic to systolic pressure is in the range of 1.5 to 2.0.[19] At the completion of ECP treatment, patients were analyzed by groups with a DA ratio of either < 1.5 or $\geq$ 1.5. Only 37% of the 1,004 study patients achieved a DA $\geq$ 1.5. Patients in the low DA group appeared to have worse clinical outcomes (unstable angina, CHF, and higher angina class, p < 0.05 or better), but baseline variables between the two groups were not reported. Factors associated with lower DA ratio included age $\geq$ 65, female gender, left ventricular ejection fraction < 35%, hypertension, prior coronary bypass surgery, noncardiac vascular disease, multivessel disease, congestive heart failure, current smoking, unsuitability for further revascularization, and higher baseline angina class. The authors stated "the incidence of congestive heart failure exacerbation and the improvement in angina class appear to be related to the degree of DA with EECP." This article concluded that "DA is important in achieving maximal clinical benefit from EECP."

A 2002 examination of IEPR data of 2,486 patients for the relationship of diastolic augmentation and clinical benefit was similar to the previous article.[20] In this study, 1,009 patients had a DA ratio below or equal to the median level both at the beginning (0.7) and end (1.0) of EECP. Some of the factors associated with a DA ratio below the median were very similar to the previous study (female gender, noncardiac vascular disease, age 65, smoking, heart failure, diabetes, hypertension, prior coronary artery bypass surgery – it was unclear what other variables were examined). The authors suggested that the patients who had the greatest increase in the DA ratio from beginning to end of treatment had the greatest reduction in angina class. Regardless of the DA ratio change (even in the 250 who after treatment went in the opposite direction – from 1.0 to 0.7), there appeared to be a response as judged by a reduction in angina class.

Stys, et al., examined the hemodynamic effect of EECP in IEPR data.[6] The authors reported that the hemodynamic effect of EECP did not predict improvement in CCS angina class (the initial and final effectiveness ratios were similar in patients with and without improvement in CCS angina class).

A 1985 study by Kern, et al., measured coronary and systemic hemodynamics before, during, and after ECP treatment in 14 patients with coronary artery disease and normal left ventricular function.[21] A triple thermistor coronary sinus thermodilution catheter introduced via an antecubital vein and a balloon-tipped pulmonary artery catheter measured right atrial, phasic, and mean pulmonary artery pressure and cardiac output, and a dual micromanomter transducer tipped catheter measured left ventricular and aortic pressures. While they found an increase in the arterial pressure (108 ± 11 to 114 ± 12 mm Hg, $p < 0.01$) and diastolic pressure-time index (440 ± 51 to 498 ± 82 units, $p < 0.01$), they found no change in the systolic pressure-time index, or absolute coronary sinus, or great cardiac vein blood flow. The authors concluded that external diastolic pressure augmentation did not affect heart rate, right heart hemodynamics, cardiac output or calculated myocardial oxygen consumption.

Canadian Cardiovascular Society Classification II (CCSC II)
The evidence presented for inclusion of CCSC II in Medicare coverage comes from two sources: 1) a 1999 subgroup analysis of the MUST-EECP study (not separately published); and 2) IEPR subgroup analysis originally from 2 year follow-up data published in 2004, with Class II data not separately published in the article.[25] CMS applies less weight to evidence that is not first published in a peer-reviewed journal. The original published 2004 study includes 1,097 registry patients from the IEPR of which 95% were white and 74% were male. Outcomes were measured by telephone follow-up. Outcomes are angina class and quality of life assessment using 5-point scales for health status, quality of life, and satisfaction with quality of life. Of the patients starting ECP, 82% completed 35 hours of therapy, with 10% and 8% discontinuing therapy because of clinical events and patient's preference. Of the total cohort immediately after completion of ECP treatment, 73% of patients had a decrease in angina class of $\geq$ 1, 26% had no change in angina class, and 1% had an increase in angina class. Fifty percent reported improved quality-of-life. At two year follow-up, 74.9% reported angina class reduction, although it is not clear how drop-outs from the start of the study or failure to follow-up was addressed. Quality-of-life assessment is reported as being sustained at the 2-year follow-up. In the 2004 article, the authors acknowledged, "A primary limitation of this analysis was the lack of a control group to assess the extent of the reported improvement due to other interventions (i.e., medical therapy, lifestyle modifications, coronary revascularization) or to a "placebo effect" that may be expected in a population of highly symptomatic patients enthusiastic for an emerging novel treatment." They also stated, "This observational registry study cannot directly evaluate whether the anti-ischemic effects observed in the randomized Multicenter Study of Enhanced External Counterpulsation trial extends to a broader population of patients treated with EECP. Self-reported severity of angina based on mail or telephone interview is subject to potential bias, although coordinators in the IPR were trained in assessing and defining follow-up symptoms."

In 2000, in a case series study of 2,289 patients from the IEPR data, CCS functional class I and II patients "were grouped together to provide a reference for this analysis because they were unable to show further improvement in functional class with treatment."[26] Patients in this study had varying treatment times (average treatment time was 33.43 ± 12.3 hr), with the author's conclusion being "the dose effects of EECP remain speculative." Characteristics of patients were 92.4% white and 79.7% male. Average age was 65.8 ± 10.7 years (range 19 years – 97 years). The average CCS anginal class before treatment of 2.78 improved to an average of 1.81 after treatment ($p < 0.001$). The authors stated that patients in CCS III and IV were significantly more likely to demonstrate functional improvement. Odds for improvement for pre-ECP CCSC IV were given as 3.30 (2.49 – 4.39) and for pre-ECP III as 4.38 (3.46 – 5.56). The odds for class I or II were not given.

Indication 2 - Heart Failure

Evidence supporting expansion of ECP to congestive heart failure includes data from the IEPR (which is used to track acute and long-term outcomes for consecutive patients treated for chronic angina), a 26 patient feasibility study in euvolemic patients, and Cardiomedics registry data. Results of the prospective evaluation of EECP in heart failure (PEECH) trial have not yet been published in a peer-reviewed journal thus less weight is being given to this evidence. Should the results be published during our comment period, CMS will review them before making a final determination.

IEPR data was used in a study published in 2001 comparing ECP outcomes for refractory angina in 548 patients with a history of congestive heart failure (CHF) to 1,409 patients without a history of CHF, looking at adverse events and CCS angina class (qualifying CHF criteria not specified).[27] The mean age of the study group was 67.1 ± 10.9 years, and 72% were male (racial/ethnic demographics not presented). Though "EECP was typically prescribed for 35 1-hour sessions over a period of 7 weeks", mean treatment hours varied, reported as 34.7 ± 10.2 hours for those without a history of CHF and 33.1 ± 10.8 hours for those with a history of CHF ($p < 0.001$). In this observational study, the history of CHF group had fewer patients complete the course of EECP (78% completed the course as prescribed versus 86% of those without a history of CHF, $p < 0.001$). Angina class improved one or more classes in 68% of the history of CHF group and in 75% in those without a history of CHF ($p < 0.01$). It worsened in 0.9%. At 6 months, patients with a history of CHF reported maintenance of reduced angina, but were more likely to report a major adverse event (death: 7.9% versus 2.2%, $p < 0.001$; cardiac hospitalization: 19.1% versus 13.6%, $p < 0.01$; major adverse cardiac event: 14.4% versus 8.6%, $p < 0.001$).

In a 2002 study of IEPR data left ventricular dysfunction was defined as ejection fraction (EF) $\leq$ 35% (recorded prior to ECP therapy, but time range of measurements not given).[28] The study included 1,402 patients with 77.7% LVEF > 35% and 22.3% LVEF $\leq$ 35%. Patient characteristics show the group with left ventricular dysfunction to have more patients in CCSC III/IV (86.2% v. 73.6%, p value not given), greater multivessel disease (89.8% v. 76.5%, $p < 0.001$), and more unstable angina (4.8% v. 1.7%, p value NS). Patients with an ejection fraction $\leq$ 35% were less likely to complete a course of treatment (79.4% vs. 85.8%, $p < 0.01$) with the reason for stopping treatment more likely to be a clinical event (14.4% vs. 7.2% with $p < 0.001$). Six-month data were available on 84% of the initial 1,402 patients. Patients with the lower EF had greater 6-month mortality (9.3%) versus those with the higher EF (2.2%, $p < 0.001$). Six month post-treatment results (for those patients reporting anginal status) include 81.0% of the $\leq$ 35% LVEF group and 83.8% of the LVEF > 35% having either no change in angina or less angina than immediately post-ECP treatment (p = NS).

A 2005 IEPR study reported data for 746 patients with angina and with a history of heart failure.[29] Patients were divided into two groups: LVEF $\leq$ 35% (diastolic dysfunction as defined by the article) and LVEF > 35% (systolic dysfunction as defined by the article). Standard ECP treatment was prescribed (35 hours, pressures not noted) with 79.3% of the diastolic dysfunction (DD) group and 76.9% of the systolic dysfunction (SD) group completing the course of treatment (p = NS). CCS anginal class was reduced by $\geq$ 1 class in 71.9% of DD patients versus 72.2% of the SD patients (no p value given), with similar decreases in anginal episodes and nitroglycerin use. No measurement of ejection fraction was made post treatment. At one year, decreased angina was reported as 78.1% of DD patients and 75.8% of SD patients as compared to pretreatment (p = NS) (not all subjects were available for the telephone follow-up). Fifteen months after the first hour of EECP, death occurred in 14.1% for the DD group and in 9.2 % of the SD group ($p = 0.039$). Major adverse events (death myocardial infarction, coronary artery bypass graft, percutaneous coronary intervention) occurred in 23.8% for the DD group and 24.4% of the SD group ($p = 0.98$).

A 2002 feasibility study for ECP treatment of NYHA class II/III was undertaken in 26 patients.[30] Exclusion criteria for this study included exercise limited by chest pain, EKG changes consistent with myocardial ischemia, unstable angina, and others. Inclusion criteria were that patients had to have the ability to exercise on a treadmill (Modified Naughton Protocol) with exertion limited by either shortness of breath or fatigue, and heart failure treatment must have been optimized and stable (demonstrated as an absence of medication changes over the 2 weeks prior to the first study visit) prior to enrollment. Age was 56.3 ± 16.1 years, with 18.8% females. Peak oxygen uptake, quality of life, and exercise duration were outcome measures. Statistical analysis was performed by comparing mean changes of the outcome measures from baseline to one-week post treatment and to the end of the study (presumed 6 month follow-up), using paired t tests. Peak oxygen uptake in 23 patients increased from the mean baseline value of 14.99 to a mean of 15.98 mL/kg/min (se ± 3.57% min - 27.09% max + 43.57%; $p = 0.05$) at one week follow-up. Nineteen patients completed the 6 month follow-up, with peak oxygen uptake increased from mean baseline of 14.78 to a mean of 18.41 mL/kg/min (se ± 34.71% min - 0.46 % max + 62.76%; $p < 0.001$). Exercise duration (unclear if this was measured in 23 subjects) increased from the baseline value of 637.63 seconds to 732.96 seconds (se ± 4.89% min - 7.66% max + 89.58%; $p < 0.001$) at one week follow-up. At 6 month follow-up (19 patients), exercise duration increased from 637.13 seconds to 715.17 seconds (se ± 6.53% min - 15.20 % max + 81.02%; $p < 0.028$). Quality of life data using the Minnesota Living with Heart Failure Questionnaire (MLHFQ) was assessed at baseline, one week post treatment follow-up (24 patients), and 6 month follow-up (22 patients). The authors reported that “the overall changes between the test results at baseline and one-week post-treatment were significant ($p < 0.01$) for total score, physical dimension and emotional dimension. In the 22 patients who completed the study and had the MLHFQ at 6-month follow-up visit, total score showed persistent improvement over baseline values, but only the change in emotional dimension remained significant ($p < 0.01$).”

A 2005 report of 127 Cardiomedics ECP registry patients examined the effect of treatment in patients with NYHA class II -IV CHF patients.[31] CHF inclusion criteria were symptoms and signs of CHF with shortness of breath, leg edema, or significant fatigue. Patients were treated with lower pressures. The authors stated “the high pressures and resulting 1.5:1 -2:1 peak diastolic to peak systolic pressure (D/S) ratios shown to be optimal in the treatment of angina can cause excessive preload and adverse effects in congestive heart failure (CHF) patients, particularly those with left ventricular ejection fractions < 40%”. In this study, pressures and resultant D/S ratios (referred to as DA ratios in other articles) started as low as 0.1:1. Patients were divided into three groups based on the post-hoc resultant average diastolic augmentation ratio. The resultant average D/S ratios in the three groups were 0.7:1 in the low group, 1.08:1 in the middle group and 1.32:1 in the high group. The outcomes examined were comparative changes in mortality, LVEF, NYHA CHF class, and incidence of all-cause hospitalizations for a period of 1 year following the therapy. For statistical purposes, measurements were mean D/S ratio, with individual variable differences determined using the Student t test and the chi-square test. As with other ECP studies, there was a preponderance of men (> 79%); race/ethnicity were not listed. Although in all three groups medical therapy is in accordance with accepted medical practice, only 55% of patients in one group were reported to receive angiotension-converting enzyme inhibitors (versus 74.4 and 81.5 in the other groups), and only 23.3 – 31.4% of enrollees received beta blockers, despite diagnoses of angina with documented evidence of coronary artery disease and CHF. Therapy breakdown one year post ECP therapy was not given. It was not stated if treatment changes (i.e. medications, lifestyle) during or after ECP were adjusted for.

Table 2. Left Ventricular Ejection Fractions of Surviving Patients

Group	*Before ECP (%)*	*Year After ECP (%)*	*p value*
Low D/S ratio(n=53)	32.6 ± 7.2	40.1 ± 26.9	< 0.05

Table 2. Left Ventricular Ejection Fractions of Surviving Patients			
Mid D/S ratio(n=36)	31.3 ± 11.6	37.5 ± 27.5	NS
High D/S ratio(n=31)	32.6 ± 20.4	38.3 ± 14.7	NS

Table 3. New York Heart Association Congestive Heart Failure Classification of Surviving Patients			
Group	*Before ECP*	*Year After ECP*	*p value*
Low D/S ratio(n=53)	3.7 ± 1.0	1.9 ± 0.5	< 0.0001
Mid D/S ratio(n=36)	2.7 ± 1.3	1.9 ± 0.5	< 0.005
High D/S ratio(n=31)	2.7 ± 1.3	1.9 ± 0.5	< 0.01

Table 4. Annual Average Number of All-Cause Hospital Admissions per Patient			
Group	*Before ECP*	*Year After ECP*	*p value*
	2.8 ± 1.6	0.35 ± 0.5	< 0.0001

Table 4. Annual Average Number of All-Cause Hospital Admissions per Patient			
Low D/S ratio(n=54)			
Mid D/S ratio(n=39)	2.5 ± 1.4	0.42 ± 0.5	< 0.0001
High D/S ratio(n=34)	1.3 ± 1.7	0.70 ± 0.5	< 0.01

The number of patients analyzed for hospital admissions was not the same as the number of patients analyzed for LVEF or NYHA class. It was not clear if the average annual number of all-cause hospital admissions per patient was adjusted for comorbidities. The incidence of all-cause hospital admission per patient was given by D/S ratio, not CHF class.

Table 5. Mortality: Comparisons Between Groups				
Study Group (NYHA Class)	Mortality (%)	Comparison Group (NYHA Class)	Mortality (%)	p value
Low D/S ratio(II-III)	0.00	MADIT II (II-III)	8.50	< 0.0001
Low D/S ratio(III-IV)	2.10	COMPANION (III-IV)	12.20	< 0.0001
Low D/S ratio(II-IV)	1.85	Mid D/S (II-IV)	7.69	< 0.0001
Low D/S ratio(II-IV)	1.85	High D/S (II-IV)	8.82	< 0.0001
	7.50	High D/S (II-IV)	8.33	NS

Table 5. Mortality: Comparisons Between Groups				
Mid D/S ratio(II-IV)				

A mortality reduction was suggested when the three D/S ratio groups were compared, i.e. low ratio compared to mid and high ratio where risk comparison is based on the post-hoc group assignment. The authors used the Multicenter Automatic Defibrillator Implantation Trial II (MADIT II) and the Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) studies for additional mortality comparisons.

CMS has been informed by Vasomedical that results of the Prospective Evaluation of EECP in Congestive Heart Failure (PEECH), which was presented at the American College of Cardiology 2005 Annual Scientific Session, have been accepted for publication. Subjects (187) with mild to moderate symptoms of heart failure were randomized to either ECP treatment (applied pressure of 300 mm Hg) and protocol-defined pharmacologic therapy (PT) or PT alone. Two co-primary end points were predefined: the percentage of subjects with a 60 second or more increase in exercise duration and the percentage of subjects with at least 1.25 ml/min/kg increase in peak VO_2(peak oxygen uptake) at six months. After six months, 35% of EECP patients and 25% or control patients increased their exercise duration by at least 60 seconds (p = 0.016). NYHA functional class improved in 31% of EECP patients compared with 16% in the control group and EECP patients reported a greater improvement in quality of life. However, there was no significant difference in peak VO_2 between the two study groups.[32]

Indication 3 - Cardiogenic Shock

Three studies were reviewed for this indication.

A 2000 study of 39 patients in Japan compared the intra-aortic balloon pump (IABP) to ECP in patients with acute myocardial infarction, after balloon coronary angioplasty.[33] Twelve patients (Killip class on admission I or II) had an IABP placed in the cardiac catheterization laboratory due to intracoronary thrombosis observed during coronary angioplasty. ECP was performed in another 27 patients (Killip class 1) 2 or 3 days after admission. Hemodynamics were measured invasively in both groups. The ECP measurements were taken at baseline and then during treatment at 15 minutes, 30 minutes, 45 minutes, 60 minutes, and 60 minutes after treatment. In the IABP group, baseline measurements were obtained > 60 minutes after setting of minimal IABP effect to achieve a static hemodynamic condition and to avoid blood clots on the IABP balloon surface. The 15, 30, 45, and 60 minute measurements were obtained after starting full support of IABP and the last measurement obtained 60 minutes after returning to a minimal IABP effect. The authors reported: "Mean values of heart rate did not change significantly in either group before, during, and after treatments. Mean values of heart rate at baseline and during and after treatments did not show significant differences between the 2 groups. Mean values of right atrial pressure increased significantly at 15 and 30 minutes after starting EECP compared with values at baseline, then decreased gradually. There was no significant increase in right atrial pressure 45 and 60 minutes after starting EECP compared with baseline value. Although mean values of right atrial pressure did not change in the IABP group, there was no significant difference at any measuring time point between 2 groups, except at 15 minutes after starting treatment. Mean values of pulmonary capillary wedge pressure in the EECP group increased significantly at 15 and 30 minutes after starting EECP, and then decreased gradually, but no significant change was seen in the IABP group. Differences of mean values between the 2 groups were not significant at baseline and during treatment. However, the mean value at 60 minutes after stopping treatment was significantly lower in the EECP group than in the IABP group. Mean values of cardiac index increased significantly at 45 and 60 minutes after starting treatment compared with the baseline value in the EECP group. However, no significant change was observed in the IABP group. The mean value of cardiac index at 60 minutes after starting treatment in the EECP group was significantly greater than that in the IABP group. Mean values of the areas under the artery pressure curves during the diastolic phase increased significantly compared with baseline value at every measurement point during treatment in the EECP group, and at 45 and 60 minutes in the IABP group. There was no significant difference between the 2 groups at any measuring point. Mean values of the areas under the artery pressure curves during the systolic phase decreased significantly during treatment compared with baseline in the IABP group. No significant change was observed, however, in the EECP group. Mean values in the IABP group were significantly lower than those in the EECP group at every measuring point during treatment. Mean values of systolic systemic vascular resistance decreased significantly during treatment compared with baseline values in both groups. No significant difference in systolic systemic vascular resistance between the 2 groups was observed at any measuring point." While outcomes were measured as hemodynamic comparisons at specified times, it was noted that measurement time from admission was not the same in the groups. Additionally, intra-aortic balloon pumps are generally administered in unstable hemodynamic states, whereas the hemodynamic state of these subjects was stable.

A 2002 case series included 10 hemodynamically stable patients who underwent left heart catheterization and coronary angiography from the right radial artery for diagnostic evaluation.[34] At baseline and then during ECP (external cuff pressures ranging from 100 to 300 mm Hg), hemodynamics were measured in unobstructed coronary arteries and included central aortic pressure (using a coronary catheter), intracoronary pressure (a sensor-tipped high-fidelity pressure guidewire), and Doppler flow velocity (a Doppler flow guidewire). ECP resulted in an increase in diastolic (71 ± 10 mm Hg at baseline to 137 ± 21 mm Hg during EECP, $p < 0.0001$) and mean intracoronary pressures (88 ± 9 to 102 ± 16 mm Hg, $p = 0.006$) and a decrease in systolic pressure (116 ± 20 to 99 ± 26 mm Hg, $p = 0.002$).

A 1974 case series study of 20 patients who were clinically diagnosed with cardiogenic shock after myocardial infarction were treated with ECP.[35] Other treatments included a transvenous pacemaker and digitalis if needed, assisted ventilation through an endotracheal tube or oxygen by mask or nasal canula, intravenous fluids and/or sodium bicarbonate if needed, metarmial bitartrate, isoproterenol, mephentemine, methylprednisoline, chlorpromazine, dexamethasone, levartarenol, and hydrocortisone. Eleven patients died during or soon after treatment. Two more patients died within 3 weeks but were counted as survivors in the analysis. Seven patients were discharged from the hospital. The study claims that the 45% survival rate with ECP (which included the two short term survivors) was an improvement ($p < 0.01$) over the usual 15% survival rate of cardiogenic shock.

Indication 4 - Acute Myocardial Infarction

A 1980 study randomized (based on allocation by a coordinating center) 258 acute myocardial infarction patients to either 4 or more hours of ECP within 24 hours of admission or to control.[36] Diagnosis of MI was on the basis of "classic history, characteristic ECG evolutionary changes and typical serum enzyme changes." Left ventricular function was judged on clinical exam and x-ray changes. Other treatment included antiarrhythmic drugs, diuretic agents, digitalis, vasodilator drugs and propranolol, and analgesic or sedative therapy. In the group receiving 4 or more hours of ECP within the first 24 hours after admission, the mortality rate was 6.5% in the treatment group versus 14.7% in the control group ($p < 0.05$). Also, for the group of patients with 3 or more hours of treatment, ECP was associated with a lower morbidity as defined by recurrent chest pain, progression of cardiac failure, occurrence of ventricular fibrillation, change in heart size and clinical cardiac functional status at discharge, with p values ranging from < 0.05 to < 0.01.

4. MCAC

The MCAC was not held for this topic.

5. Evidence-based Guidelines

The American College of Cardiology/American Heart Association (ACC/AHA) 2002 "Guideline Update for the Management of Patients with Chronic Stable Angina-Summary Article" is a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. The level of evidence assigned to ECP is Class IIb, "usefulness/efficacy is less well established by evidence/opinion", which is their lowest level of evidence suggesting there may be some benefit. It is further stated "additional clinical trial data are necessary before this technology can be recommended definitely."[37]

In "Primary care management of chronic stable angina and asymptomatic suspected or known coronary artery disease: a clinical practice guideline from the American College of Physicians", under alternative therapies for patients with refractory angina, "evidence is still lacking for the use of …, enhanced external counterpulsation…" Additionally stated, "these techniques should be used only in patients who cannot be managed adequately by medical therapy and who are not candidates for revascularization (interventional or surgical)."[38]

The ACC/AHA 2005 Guidelines for the Evaluation and Management of Chronic Heart Failure in the Adult states: "External Counterpulsation. The technique of external counterpulsation involves the use of a device with inflatable cuffs that surround the lower limbs and inflate and deflate in synchronization with the cardiac cycle. The device is designed to reduce loading conditions in systole while increasing coronary perfusion pressures in diastole. External counterpulsation has been shown to reduce the frequency and severity of anginal attacks in patients with symptomatic coronary artery disease. A possible mechanism of action for its observed clinical effect may be an improvement in endothelial function of the coronary vascular bed. Early trials of this therapy in patients with HF and low EF have been encouraging, and a randomized trial has been completed recently. Until more data are available, routine use of this therapy cannot be recommended for the management of patients with symptomatic reduced LVEF." [39]

The ACC/AHA does not mention external counterpulsation in the guidelines for acute myocardial infarction management.[40]

In the emergency management of patients with cardiogenic shock algorithm, ECP is not listed.[41]

6. Professional Societies

The American College of Cardiology, in response to CMS' request for public comments on the proposed expansion of ECP coverage, stated: "CMS requested public comment on whether evidence is adequate to evaluate health outcomes of ECP for the following indications: Class II angina; NYHA class II/III stable heart failure symptoms with an ejection fraction $\leq$ 35%; stable heart failure with an ejection fraction $\leq$ 40%; acute heart failure; acute myocardial infarction; cardiogenic shock. The College does not believe the evidence now available is adequate to evaluate the health outcomes of ECP for the conditions listed above. We understand, however, that results of an ongoing clinical trail of ECP may soon be published. CMS may wish to evaluate those data when they become available."

7. Expert Opinion

Three primary authors of ECP studies provided comment. Dr. William Lawson and Dr. Andrew Michaels wrote in support of expanding coverage to include patients with CCSC II angina pectoris and those with class II/III heart failure due to left ventricular systolic dysfunction. Dr. Kris Vijayaraghavan wrote in support of treatment of CCSC II angina pectoris and the graduated pressure regimen for patients with NYHA Class II, III and IV congestive heart failure.

8. Public Comment

CMS requested public comment on the following issues, as well as any others of concern to the public, during the initial 30 day public comment period:

Is the evidence adequate for evaluating health outcomes of ECP for the following indications?

- Class II angina
- NYHA Class II/III stable heart failure symptoms with an ejection fraction ≤ 35%
- Acute heart failure
- Acute myocardial infarction
- Cardiogenic shock
- Stable heart failure with an ejection fraction ≤ 40%

In addition, we requested public comment on the following 2 questions:

- For each listed condition, is the evidence sufficient to evaluate the effectiveness of ECP for treatment of patients as an adjunct or alternative to a surgical intervention?
- Is the evidence sufficient to determine the effectiveness of ECP graduated low pressure regimen as compared to the standard ECP pressure regimen in the treatment of patients with congestive heart failure?

General Public

A total of eighty comments were received.

Seventy-nine comments were received in support of the use of external counterpulsation therapy. The comment sources included patients who had received ECP treatment and those involved in providing the service of ECP therapy which included nurses, ECP therapists, physicians, program managers, and stakeholders in the ECP operations. Grouping comments by indication resulted in the following:

Angina treatment,

- Support was offered for covering CCSC II (15 total) by nine physicians who provide ECP treatment and nine other commentors including an ECP coordinator, a director of cardiopulmonary services, and a company CEO;
- CCSC I and II were supported by three providers involved in ECP treatment;
- Treatment of angina in general was supported by eight physicians, several nurses, and others.

Congestive heart failure,

- Support was offered for covering NYHA Class II and III by 11 commentors, six of whom were physicians who provide ECP treatment;
- Treatment of CHF with low pressure regime was supported by two commentors, one of whom identified himself as a physician;
- Treatment of acute heart failure was supported by two physicians;
- Sixteen physicians and 21 others including nurses, ECP therapists, and patients offered general support for the treatment of congestive heart failure.

Additionally, seventeen commentors including seven physicians expressed broad support for ECP treatment.

Support was based generally on opinion and anecdotal evidence, with no new evidence in the form of peer reviewed published articles being presented. In support of ECP treatment, a common sentiment of providers currently involved with ECP was that current patients had improvements in exercise tolerance, general quality of life, and a reduction of other symptoms. One commentor noted, “Currently Medicare only allows for coverage of this therapy for Class II [sic] & IV angina. … this particular group of patients with co-existing CHF, have done extremely well with EECP therapy.” Several commentors offered similar observations that “this therapy along with all the accompanying patient education on lifestyle modification, diet, medications, activity; along with daily monitoring of patients allowing us to fine tune their medications appropriately have shown me that the majority of patients will benefit”. Similarly, “Our therapy program includes teaching of our patients with referrals from dietary, pharmacy, and pulmonary rehab for smoking cessation, as needed.”

Other comments included: “It is vastly more effective than any of the invasive treatment and considerably more cost effective”; “…many elderly patients would be better served by receiving outpatient EECP rather than being hospitalized for CHF treatment, angiography, or high risk revascularization procedures.” One commentor stated, “EECP costs $5,000 -a bargain compared to angioplasties, bypasses and repeated hospitalizations”, while another commented, “The medical community has not embraced this noninvasive therapy due to its restrictive coverage policy and for many, the cost and effort for providing therapy is not worth the reimbursement provided.” Some felt that primary care physicians who manage these patients should be able to prescribe this therapy.

One commentor said there was no evidence of any benefit.

While public comments from providers and patients of personal experiences are informative, our NCDs rely on published, scientific evidence in making coverage decisions. We did not receive any additional evidence during this comment period.

VIII. CMS Analysis

National coverage determinations (NCDs) are determinations by the Secretary with respect to whether or not a particular item or service is covered nationally under Title XVIII of the Social Security Act § 1869(f)(1)(B). In order to be covered by Medicare, an item or service must fall within one or more benefit categories contained within Part A or Part B, and must not be otherwise excluded from coverage. Moreover, with limited exceptions, the expenses incurred for items or services must be "reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member." § 1862(a)(1)(A). This section presents the agency's evaluation of the evidence considered and conclusions reached for the assessment questions.

CMS focused on this general question for the listed indications:

Is the evidence sufficient to conclude that as a result of treatment with external counterpulsation the Medicare population will have net health benefits for the following conditions?

- Canadian Cardiovascular Society Classification (CCSC) II angina
- Heart Failure - New York Heart Association Class II/III stable heart failure symptoms with an ejection fraction of $\leq$ 35%
  - New York Heart Association Class II/III stable heart failure symptoms with an ejection fraction of $\leq$ 40%
  - New York Heart Association Class IV heart failure
  - Acute heart failure
- Cardiogenic shock
- Acute myocardial infarction

General Issues

Study design is important for convincing and dependable outcome results. Case series do not provide evidence about whether the treatment itself directly causes the subsequent outcome, or whether some other concurrent factor is responsible for the observed outcome (or, to what extent each factor contributes, if any contribution is made, to the outcome). The type of study that reports what is observed, without a comparative control group, deserves less weight than those studies that do have a comparison group because all the potential events that can occur during treatment, including those caused by additional therapies, can not be separated from the overall effect. Because of this study design, one is left with uncertainty about which factor of the many that goes into the complex interaction of patient, treatment and disease, produced the reported result. Placebo effect is a consideration, therefore convincing and dependable outcome results are needed to dispel this possibility. Factors that reliably affect morbidity and mortality are outcome results of interest to CMS. When surrogate outcomes of uncertain clinical significance are chosen by investigators in the design of a study, those outcomes are rarely useful in making a determination of reasonable and necessary.

Is the evidence sufficient to conclude that as a result of treatment with external counterpulsation therapy the Medicare population will have net health benefits for stable angina?

Most of the published studies are of patients with stable angina. No separate studies on Class II angina have been published. An ad-hoc subgroup analysis has been presented as evidence. Examining the evidence for stable angina, most of the published available evidence is limited by lack of a comparison group. It is difficult to rely on observational evidence when there is no comparison group to say that one specific treatment is effective when there are many concurrent changes. Therefore, much of the best evidence rests on the MUST-EECP trial. This trial had many exclusion criteria, which limit the generalizability of the results to other patients. In this study, there was a significant drop-out rate, with a lack of detail as to why the patient dropped out. Those patients were not included in the analysis. Given the high drop-out rate, it is unclear if those who were having a poor response were the ones that dropped out, thus producing bias. When intention to treat analysis is applied, only 56 patients out of 71 randomized were analyzed. Intention to treat analysis is a strategy for analyzing data from a randomized controlled trial. All participants are included in the group to which they were allocated, whether or not they received or completed the treatment given to that group. When participants are excluded, the premise of an equal baseline between the two groups is disrupted, and the validity of the evidence is lessened. There is uncertainty regarding the clinical significance of the reported improvement in physiologic measures. While exercise capacity (maximal oxygen uptake for a given workload, expressed in metabolic equivalents) has been shown to be an independent predictor of risk of death and cardiac events among asymptomatic women and men, the clinical benefit of a 49 second increase in time to ST-segment depression is unclear in those with chronic angina. Thus, a surrogate outcome such as this is difficult to assess in determining reasonable and necessary. The rationale for method of analysis is not always clear. For instance, what is the clinical significance when assessment by mean angina counts is not statistically significant, but an analysis using categories of percentage improvement shows statistical significance? Is the point of statistical significance the primary interest? The other two measures, nitroglycerin usage and exercise duration, showed no difference between groups. While ECP has been described as safe, in the randomized study, 55% of the ECP patients had adverse experiences as compared to 26% in the sham treatment group.

The subsequent quality of life study included only 54% of the original participants. It is not clear how these patients differed from the rest of the original group, again introducing selection bias. How would the results change if all of the original patients were included? Questionnaire score changes are presented without baseline scores, creating difficulty in interpretation for the reader. Other limitations include small sample size (low power to detect differences), quality of life data not being correlated with the previous data from exercise testing, anginal symptoms, or the anginal episodes for the one year outcome. When results such as this are not presented, one is left wondering if those that showed improvement in other measures in the MUST-EECP trial may not have shown an improvement in quality of life. It is unclear why this correlation was not done.

The remainder of the studies are small case series and reports of registry data. For both types of studies, there is no comparison group, so it is difficult to determine if improvement is due to ECP. Though the results appear positive, the method of data collection (where there is no comparison group and it is unclear what patients were excluded) biases these results. Some articles suggest that the placebo effect may be important. It has been reported that the use of medical devices may be associated with an enhanced placebo effect.[42] While the placebo effect remains enigmatic, it can be robust, and angina is known to have a high placebo response.[43] In a study population of patients with coronary heart disease, placebo effects were found to have longevity.[43] This effect is not limited to symptomatic endpoints, but also to end points such as exercise time and magnetic resonance imaging, though it is not clear why this happens. Having a net benefit over time does not rule out the placebo effect, as the benefits of placebo therapy on coronary heart disease have been shown to persist for at least as long as 2 years.[43] Another important registry issue is that follow-up is done by phone based on the patient's self report, and is subject to recall bias.

General effects not specific to angina may also be important with ECP therapy and cannot be excluded given the existing literature. Close medical attention is provided at specific centers, with prolonged duration of treatment, which may have a significant effect in reducing the symptoms of treated patients through various mechanisms. These factors may include better patient compliance with drug treatment regimes, closer adherence to treatment guidelines among treating physicians, accompanying patient education on lifestyle modification, diet, medications, and physical activity, as well as motivated patients.

While the hemodynamic effects of ECP are dependent on the magnitude of applied external pressure, symptoms in patients with angina improved even in the absence of an optimal hemodynamic effect, which also suggests that nonspecific effects may contribute to the symptomatic benefit of EECP.[5,6,44] Additionally, if hemodynamics are important it is not intuitive that when the DA ratio falls rather than increases, an improvement is shown. From this, it would appear that DA ratio does not have an effect on symptoms. While ECP has been found to cause acute changes in hemodynamics, there have been no studies of chronic changes in hemodynamics following ECP. Importantly, hemodynamic measurements do not take the place of accepted measures, such as angiography, for cardiovascular disease.

In case series studies (including registry data), morbidity and mortality data without a comparable study comparison is difficult to evaluate. Comparison between studies with different selection criteria and indications, data quality and completeness, and historical point in time is problematic at best for comparison of a treatment benefit estimate between the two groups. Narrowly focused morbidity reporting may miss important treatment related effects.

An issue related to the possibility of a training effect on skeletal muscle made possible by a placebo effect on chest pain leads to a similar exercise-related question particularly in Class II angina patients – those who have angina only with strenuous exercise. ECP has been reported to have effects similar to physical training.[44,45,46] It is not clear how the effects of ECP are different from exercise in patients who can participate in physical conditioning. In other words, will an exercise program of walking achieve similar results?

In summary, the evidence was not adequate to support a net health benefit for treatment with the external counterpulsation device of Canadian Cardiovascular Society Classification II angina.

Is the evidence sufficient to conclude that as a result of treatment with external counterpulsation the Medicare population will have net health benefits for heart failure?

Published evidence on the use of ECP therapy to treat heart failure includes data from a small case series feasibility study (between 19 and 24 patients) and data from a registry (about 1,385 patients with a history of heart failure or EF $\leq$ 35% who completed ECP therapy), which is used to track acute and long-term outcome for consecutive patients treated for chronic angina. Although we reviewed unpublished data, less weight is given to this evidence. As with the same registry data for stable angina, there are significant methodological problems, such as suggesting direct risk comparison between different studies and no clear statement of adjustment for comorbidities or treatment changes. Additionally, it is not clear if those who are not included in the results differ from those who are excluded. Though the results of these case series studies again appear positive, the method of data collection limits any reliable conclusions. One device firm suggests that standard therapy pressures (e.g. up to 300 mm Hg) are appropriate treatment for congestive heart failure, while another device firm claims that higher pressures are harmful in CHF, suggesting that graduated lower pressures are the appropriate therapy. These two ideas would appear mutually exclusive. A comparison trial would best address this question.

In summary, the evidence was not adequate to support a net health benefit for treatment of heart failure with the external counterpulsation device.

Is the evidence sufficient to conclude that as a result of treatment with external counterpulsation the Medicare population will have net health benefits for cardiogenic shock?

Cardiogenic shock is a life-threatening hemodynamically unstable state. The body of evidence to support the use of ECP for this indication consists of a small case series from 1974 and also two more current small case series in hemodynamically stable patients, not in patients who have a life-threatening hemodynamically unstable state. The results of these studies may suggest that ECP is comparable to IABP treatment in certain limited circumstances, but not for the current treatment of cardiogenic shock. A study comparing prevailing therapies in hemodynamically unstable patients has not been presented as evidence.

In summary, the evidence was not adequate to support a net health benefit for treatment of cardiogenic shock with the external counterpulsation device.

Is the evidence sufficient to conclude that as a result of treatment with external counterpulsation the Medicare population will have net health benefits for acute myocardial infarction?

Much has changed in both the definition and the care of this illness since the study using ECP therapy was published in 1980.[47] Patients who in 1980 met the criteria for acute MI may not meet the current diagnostic criteria. The standard of care for acute MI has changed since 1980, so it is doubtful that clinicians would apply the same manner of therapy as they did in 1980. Though the 1980 study results may suggest that ECP treatment may have positively impacted morbidity and mortality in acute myocardial infarction, results of this study are not relevant considering the current standard of care.

Thus, we do not believe that there is adequate evidence to support a net health benefit for treatment of acute myocardial infarction with the external counterpulsation device.

Conclusions

While there have been many articles published on the topic of ECP, the data consists of one published randomized controlled trial (139 enrolled), an unpublished randomized controlled trial, nonrandomized small case series studies, various analyses of the > 5,000 patients entered into the EECP registry, and one study of the Cardiomedics registry. The accumulated data do support the current usage in those who are not amenable to surgical intervention, but cannot support the expansion of coverage. Observational studies can assess the strengths and weaknesses of the treatment under study, but cannot test the key hypotheses.

IX. Proposed Decision

The Centers for Medicare and Medicaid Services (CMS) proposes that the evidence is not adequate to conclude that external counterpulsation therapy is reasonable and necessary for:

- Canadian Cardiovascular Society Classification (CCSC) II angina
- Heart Failure - New York Heart Association Class II/III stable heart failure symptoms with an ejection fraction of ≤ 35%
  - New York Heart Association Class II/III stable heart failure symptoms with an ejection fraction of ≤ 40%
  - New York Heart Association Class IV heart failure
  - Acute heart failure
- Cardiogenic shock
- Acute myocardial infarction

Current coverage as described in Section 20.20 of the NCD manual will remain in effect.

Appendices [PDF, 599KB]
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